Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Table 4. What to Start: Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (Last updated December 12, 2019; last reviewed: December 12. 2019) (page 1 of 4)

Recommendations for initial therapy are intended for pregnant women **who have never received ART or ARV drugs for prophylaxis** (i.e., women who are ARV-naive) and who have no evidence of significant resistance to regimen components (also see Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs and Table 5).

In general, the Panel recommends that **women who are already on fully suppressive ART regimens when pregnancy occurs should continue to use those regimens**, unless they are receiving an ARV drug or ART regimen that is not recommended for use in adults or there are concerns about safety and inferior efficacy during pregnancy (see Table 5 and Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy). Clinicians may need to consider additional factors when initiating ART in women who previously received ART or ARV drugs for prophylaxis (see Pregnant Women Living with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications and Table 5).

Regimens are listed alphabetically within each drug class and recommendation category, and the order does not indicate a ranking of preference. In addition, the Panel makes no recommendation of one agent or regimen over another within each category (*Preferred* or *Alternative*).

Note: For more information about the use of specific drugs and dosing in pregnancy, see Table 5, the individual drug sections in Appendix B, and Table 8.

Drug or Drug Combination	Comments
Preferred Initial Regimens in Pregnancy Drugs or drug combinations are designated as *Preferred* for therapy in pregnant women when clinical trial data in adults have demonstrated efficacy and durability with acceptable toxicity and ease of use, and pregnancy-specific PK data are available to guide dosing. In addition, the available data must suggest a favorable risk-benefit balance for the drug or drug combination compared to other ARV drug options; the assessment of risks and benefits should incorporate outcomes for women, fetuses, and infants. Some *Preferred* drugs or regimens may have minimal toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy).	
Preferred Dual-NRTI Backbones	
ABC/3TC	Available as an FDC. Can be administered once daily. ABC **should not be used** in patients who test positive for HLA-B*5701 because of the risk of developing a hypersensitivity reaction. ABC/3TC administered with ATV/r or EFV is not recommended if pretreatment HIV RNA is >100,000 copies/mL.
TDF/FTC ***or*** **TDF/3TC**	TDF/FTC is available as an FDC. Either coformulated TDF/FTC or separate doses of TDF and 3TC can be administered once daily. TDF has potential renal toxicity; thus, TDF-based, dual-NRTI combinations should be used with caution in patients with renal insufficiency.
Preferred INSTI Regimens	
DTG/ABC/3TC (FDC) ***or*** **DTG plus a Preferred Dual-NRTI Backbone**[a]	Administered once daily. The use of DTG/ABC/3TC requires HLA-B*5701 testing, because this FDC contains ABC. INSTI-based regimens may be useful when drug interactions or the potential for preterm delivery with a PI-based regimen are a concern. In nonpregnant adults, DTG is associated with lower rates of INSTI resistance than RAL; like RAL, DTG has been shown to rapidly decrease viral load in ARV-naive pregnant women who present to care later in pregnancy. DTG is *Preferred* for the treatment of pregnant women with acute HIV infection and for women who present to care late in pregnancy. There are specific timing and/or fasting recommendations if DTG is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8). The use of DTG at conception and in very early pregnancy has been associated with a small but statistically significant increase in the risk of NTDs; this information should be discussed with patients to ensure informed decision-making. For more information, see Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy, Table 5, Teratogenicity, and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

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Drug or Drug Combination	Comments
RAL plus a Preferred Dual-NRTI Backbone	PK data are available for RAL use in pregnancy, and experience with use in pregnancy is increasing. RAL has been shown to produce rapid viral load decline to undetectable levels in women who present for initial therapy late in pregnancy. INSTI-based regimens may be useful when drug interactions or the potential for preterm delivery with PI-based regimens are a concern. Twice-daily dosing required. There are specific timing and/or fasting recommendations if RAL is taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
Preferred PI Regimens	
ATV/r plus a Preferred Dual-NRTI Backbone	Once-daily administration. Extensive experience with use in pregnancy. Maternal hyperbilirubinemia; no clinically significant neonatal hyperbilirubinemia or kernicterus reported, but neonatal bilirubin monitoring is recommended. Cannot be administered with PPIs. Specific timing recommended for dosing with H2 blockers (see Table 8).
DRV/r plus a Preferred Dual-NRTI Backbone	Better tolerated than LPV/r. Experience with use in pregnancy is increasing. Must be used twice daily in pregnancy.
Drug	**Comments**
Alternative Initial Regimens in Pregnancy Drugs or drug combinations are designated as *Alternative* options for therapy in pregnant women when clinical trial data in adults show efficacy and the data in pregnant individuals are generally favorable but limited. Most *Alternative* drugs or regimens are associated with more PK, dosing, tolerability, formulation, administration, or interaction concerns than those in the *Preferred* category, but they are acceptable for use in pregnancy. Some *Alternative* drugs or regimens may have known toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive. Therefore, it is important to read all the information on each drug in the Perinatal Guidelines before administering any of these medications to patients (also see Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy).	
Alternative Dual-NRTI Backbones	
ZDV/3TC	Available as an FDC. Although not recommended for initial therapy in nonpregnant adults, ZDV/3TC is the NRTI combination with most experience for use in pregnancy. It has the disadvantages of requiring twice-daily administration and having an increased potential for hematologic toxicities and other toxicities.
Alternative PI Regimens	
LPV/r plus a Preferred Dual-NRTI Backbone	Abundant experience and established PKs in pregnancy. More nausea than with *Preferred* agents. Twice-daily administration. A dose increase is recommended during the third trimester (see Table 8). Once-daily LPV/r **is not recommended** for use in pregnant women.
Alternative NNRTI Regimens	
EFV/TDF/FTC (FDC) ***or*** **EFV/TDF/3TC (FDC)** ***or*** **EFV plus a Preferred Dual-NRTI Backbone**	Birth defects have been reported in primate studies of EFV, but there has been no evidence of an increased risk of birth defects in human studies and extensive experience in pregnancy; cautionary text remains in package insert (see Teratogenicity and Table 8). These regimens are useful for women who require treatment with drugs that have significant interactions with *Preferred* agents, or who need the convenience of a coformulated, single-tablet, once-daily regimen and are not eligible for DTG or RPV. Screening for antenatal and postpartum depression is recommended. Higher rate of adverse events than some *Preferred* drugs.
RPV/TDF/FTC (FDC) ***or*** **RPV plus a Preferred Dual-NRTI Backbone**	RPV **is not recommended** in patients with pretreatment HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm^3. Do not use with PPIs. PK data are available for pregnant individuals, but there is relatively little experience with use in pregnancy. PK data suggest lower drug levels and risk of viral rebound in second and third trimesters; if used, consider monitoring viral load more frequently. Should be taken with food. Available in a coformulated, single-tablet, once-daily regimen.
Drug	**Comments**
Insufficient Data in Pregnancy to Recommend for Initial Regimens in ART-Naive Women These drugs are approved for use in adults but lack adequate pregnancy-specific PK or safety data.	
BIC/TAF/FTC (FDC)	No data on the use of BIC in pregnancy. Limited data on the use of TAF in pregnancy.

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Drug	Comments
DOR	No data on the use of DOR in pregnancy.
IBA	No data on the use of IBA in pregnancy.
TAF/FTC (FDC) ***or*** **RPV/TAF/FTC (FDC)**	Plasma TAF exposures in pregnant adults are similar to those seen in nonpregnant adults, whether TAF is administered with a boosting agent or not. TAF has been studied in pregnant women, but data are not yet sufficient to recommend initiating TAF in pregnancy.
Drug	**Comments**
Not Recommended for Initial ART or Use in Pregnancy These drugs and drug combinations are recommended for use in adults but **are not recommended** for use during pregnancy because of concerns about maternal or fetal safety or inferior efficacy, including viral breakthroughs in the second and third trimester (see Table 5 and Table 8). **Note:** When a pregnant woman presents to care while virally suppressed on one of these drugs or drug combinations, providers should consider whether to continue her current regimen or switch to a recommended ART regimen (see Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy and Table 5).	
ATV/c	Limited data on the use of ATV with COBI in pregnancy. Substantial reductions in trough levels of ATV in the second and third trimesters have been reported when taken with COBI.
DRV/c (FDC) ***or*** **DRV/c/FTC/TAF (FDC)**	Limited data on use of DRV with COBI in pregnancy. Inadequate levels of both DRV and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Insufficient data about the use of TAF in pregnancy (see above).
EVG/c/FTC/TAF (FDC)	Limited data on use of EVG with COBI and insufficient data on the use of TAF in pregnancy (see above). Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
EVG/c/FTC/TDF (FDC)	Limited data on use of EVG with COBI in pregnancy. Inadequate levels of both EVG and COBI in second and third trimester, as well as viral breakthroughs, have been reported. Specific timing and/or fasting recommendations, especially if taken with calcium or iron (e.g., in prenatal vitamins; see Table 8).
Drug	**Comments**
Not Recommended for Initial ART in Pregnancy and Not Recommended Except in Special Circumstances for Treatment-Experienced Women in Pregnancy These drugs **are not recommended** for use in pregnant women who have never received ART. With the exception of NVP, data about the PKs, safety, and efficacy of these drugs during pregnancy are limited. Some of these drugs are also categorized as not recommended except in special circumstances during pregnancy, because the Panel recognizes that there may be circumstances where pregnant women who are ART-experienced may need to initiate or continue these drugs to reach or maintain viral suppression (see Table 5).	
ETR	Not recommended for use in ART-naive populations. Available PK data suggest that using the standard adult dose is appropriate for pregnant patients, although data about use in pregnancy are limited.
MVC	Not recommended for use in ART-naive populations. MVC requires tropism testing before use. Available PK data suggest that using the standard adult dose is appropriate for pregnant patients, although data about use in pregnancy are limited.
NVP	Not recommended because of the potential for adverse events, complex lead-in dosing, and low barrier to resistance. NVP should be used with caution when initiating ART in women with CD4 counts >250 cells/mm^3. Use NVP and ABC together with caution; both can cause hypersensitivity reactions in the first few weeks after initiation.
T-20	Not recommended for use in ART-naive populations.

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[a] The decision to designate DTG as a *Preferred* ARV drug for therapy in pregnant women, irrespective of trimester, was based on several factors. First, DTG is associated with higher rates of virologic suppression, faster rates of viral load decline, and a higher genetic barrier to drug resistance than other *Preferred* and *Alternative* agents. Second, a recent study that evaluated a large number of pregnancies has shown that the risk of NTDs is lower than previously reported in preliminary data. This risk is also largely limited to a short period of time (before 6 weeks post-last menstrual period). A very small minority of women with HIV initiate their first ART regimen during this period of time. Some Panel members would avoid using DTG in women who are initiating ART before 6 weeks gestation. After this time, any additional risk of NTDs due to DTG is minimal. Third, data are extremely limited on the risks that are associated with using other *Preferred* and *Alternative* ARV drugs preconception or in very early pregnancy; this lack of data does not indicate either the presence or absence of risk when using alternatives to DTG. DTG is recommended as an *Alternative* agent for people who are trying to conceive, as these patients have more time to achieve virologic suppression on regimens that do not contain DTG. For additional information, see Teratogenicity, Updated Guidance About the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs in Pregnancy, and Appendix D: Dolutegravir Counseling Guide for Health Care Providers.

Note: The following drugs and drug combinations (that are not listed above) should not be used during pregnancy; if women become pregnant while taking these medications, they should switch to a recommended regimen: d4T, ddI, FPV, FPV/r, IDV, IDV/r, NFV, RTV (as the sole PI), SQV, SQV/r, TPV, TPV/r, two-drug ART regimens, or a three-NRTI ART regimen (e.g., ABC/ZDV/3TC). See Archived Drugs in the Perinatal Guidelines and What Not to Use in the Adult and Adolescent Antiretroviral Guidelines for individual ARV drugs, ARV combinations, and ART regimens that are not recommended or that should not be used in adults.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte cell; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; NVP = nevirapine; the Panel = the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine